Cardiovascular Risk Factors in Schizophrenia: A sex- and Illness Duration–Stratified Analysis

Findings from a Prospective Cohort Study

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Abstract

Schizophrenia is linked to a 15–20-year reduction in life expectancy compared with the general population, primarily due to increased cardiovascular morbidity and mortality [1, 2]. In this prospective cohort study of 235 patients with schizophrenia or schizoaffective disorder recruited at Aalborg University Hospital (Region North, Denmark), we evaluated baseline cardiovascular risk profiles, medication patterns, and psychiatric symptom severity, stratifying patients by sex and time duration since diagnosis. The cohort consisted of 103 women and 132 men, further subdivided into an early-stage group (diagnosis <2 years, n = 70) and a chronic group (diagnosis ≥10 years, n = 165).

In the overall cohort, men exhibited significantly higher cardiovascular risk markers compared with women. Men had a median systolic blood pressure of 131 mmHg versus 119.5 mmHg in women ($p < 0.0001$) and diastolic pressure of 84 mmHg versus 81 mmHg ($p = 0.0023$). Men also showed a less favorable lipid profile, with median total cholesterol at 4.8 mmol/L versus 4.4 mmol/L in women ($p = 0.0021$), LDL cholesterol at 2.6 mmol/L versus 2.3 mmol/L ($p = 0.0012$), and triglycerides at 2.0 mmol/L versus 1.5 mmol/L ($p = 0.0033$), while HDL cholesterol was significantly lower in men (1.1 mmol/L vs. 1.3 mmol/L, $p < 0.0001$).

In the early-stage subgroup, men (median age 26.5 years) were significantly older than women (median age 21.5 years, $p < 0.0001$) and demonstrated near-universal antipsychotic use (97.4% vs. 78.1%, $p = 0.0320$). Early-stage men had higher systolic blood pressure (median 130 mmHg vs. 113 mmHg, $p < 0.0001$) and a more adverse lipid profile with lower HDL (median 1.0 mmol/L vs. 1.2 mmol/L, $p = 0.0295$) and higher triglycerides (median 2.4 mmol/L vs. 1.6 mmol/L, $p = 0.0430$).

In the chronic subgroup, despite women being significantly older (median 53 vs. 48 years, $p = 0.0032$), men maintained significantly higher blood pressures and less favorable lipid profiles. Women in this group were more frequently treated with antidepressants, particularly SSRIs (49.3% vs. 31.9%, $p = 0.0356$).

Psychometric assessments (PANSS, CGI, GAF) revealed no significant gender differences, suggesting that the cardiovascular disparities are independent of psychosis severity. These findings indicate that men with schizophrenia possess a higher cardiovascular risk profile from early stages, underscoring the need for early, gender-specific cardiovascular screening and interventions. Longitudinal follow-up every three years will further clarify the impact on long-term outcomes and mortality.

Introduction

Schizophrenia is a chronic psychiatric disorder marked by a constellation of positive symptoms (e.g., hallucinations, delusions, disorganized thinking), negative symptoms (e.g., apathy, reduced emotional expression, social withdrawal), and cognitive impairments [9, 12]. Epidemiological studies have consistently demonstrated that individuals with schizophrenia have a significantly reduced life expectancy—often by 15–20 years—compared with the general population. This premature mortality is largely attributable to cardiovascular disease (CVD) and related metabolic abnormalities [1,3].

Multiple factors contribute to the increased cardiovascular risk observed in schizophrenia. Unhealthy lifestyle behaviors, including a high prevalence of smoking, sedentary behavior, and poor dietary habits, are common [13, 16]. Additionally, antipsychotic medications, particularly second-generation agents, are well documented to induce weight gain, dyslipidemia, and insulin resistance [4, 5]. Furthermore, social disadvantages and barriers to accessing primary medical care exacerbate the underdiagnosis and undertreatment of cardiovascular risk factors [8, 2].

Recent research has begun to explore whether gender plays a pivotal role in the metabolic and cardiovascular risk profiles of patients with schizophrenia. In the general population, extensive epidemiological studies have shown that men tend to develop cardiovascular disease (CVD) at a younger age than women, often exhibiting higher blood pressure and a less favorable lipid profile characterized by higher levels of low-density lipoprotein (LDL) cholesterol and triglycerides, and lower high-density lipoprotein (HDL) cholesterol [10, 14]. These sex-specific differences in cardiovascular risk factors are thought to arise from both biological and behavioral factors, including hormonal influences, genetic predispositions, lifestyle habits, and environmental exposures [4].

In schizophrenia, emerging evidence suggests that these gender differences may be even more pronounced. Men with schizophrenia might demonstrate a more adverse metabolic profile early in the course of the disorder, potentially due to a higher prevalence of risk behaviors such as smoking, poor diet, and reduced physical activity, in addition to the metabolic side effects of antipsychotic medication [6]. For example, several studies have documented that male patients with schizophrenia have higher blood pressure and a greater incidence of dyslipidemia compared with their female counterparts [7]. Furthermore, research indicates that metabolic syndrome—a cluster of conditions including central obesity, hypertension, dyslipidemia, and insulin resistance—is more frequently observed among men with schizophrenia, contributing to an increased risk of coronary artery disease and stroke [2, 1].

Conversely, women with schizophrenia are more likely to be prescribed antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs), which might reflect a higher prevalence or better recognition of depressive symptoms in female patients [8]. Such treatments may influence metabolic parameters differently, potentially offering some protective benefits in terms of lipid metabolism, although this remains an area of active investigation [5]. Moreover, sex-related differences in the presentation and treatment of schizophrenia have been linked to variations in neuroendocrine function, stress responses, and even genetic expression, all of which could modulate cardiovascular risk independently of traditional factors [12, 9].

A critical unanswered question is whether these observed differences in cardiovascular risk factors are present from the onset of schizophrenia or if they develop as a consequence of chronic illness and long-term exposure to antipsychotic medications. It remains unclear whether the metabolic disturbances in men are an intrinsic aspect of the early disease process or the result of cumulative lifestyle and treatment factors over time. Furthermore, while some studies have shown that the metabolic risks in schizophrenia are similar to those in the general population, there is growing evidence that the interplay between schizophrenia and cardiovascular disease may be more complex, with severe mental illness (SMI) itself acting as an independent risk factor for CVD [1].

To address these gaps, the current study was designed to stratify a cohort of patients with schizophrenia by both sex and time since diagnosis. By comparing an early-stage group (diagnosis within the past 2 years) with a chronic group (diagnosis ≥10 years), our aim was to determine whether sex-specific differences in cardiovascular risk factors are evident from the onset or if they emerge and intensify over time. This approach will help elucidate whether early targeted interventions might be particularly beneficial for one sex over the other, and whether such interventions could modify the risk trajectory for cardiovascular disease in schizophrenia [4, 6].

Understanding these differences is critical, given that cardiovascular disease is the leading cause of premature death in patients with schizophrenia [2]. By clarifying how metabolic risk factors differ by sex and illness duration, our study aims to inform clinical guidelines and interventions that are sensitive to the unique needs of men and women with schizophrenia, ultimately contributing to improved long-term outcomes and reduced cardiovascular mortality in this vulnerable population [1, 11].

In this study, 235 patients with schizophrenia or schizoaffective disorder were recruited from a university hospital setting. We divided the cohort into an early-stage group (diagnosed within the past 2 years) and a chronic group (diagnosed for 10 or more years). Baseline assessments included comprehensive cardiometabolic evaluations—such as measurements of blood pressure, body mass index (BMI), and lipid profiles—alongside detailed psychiatric evaluations using the Positive and Negative Syndrome Scale (PANSS), Clinical Global Impression (CGI), and Global Assessment of Functioning (GAF). Our primary objective was to determine whether men exhibit a more adverse cardiovascular risk profile than women at both early and chronic stages of illness, and whether these differences correlate with psychotic symptom severity.

This investigation is important as it provides insights into whether early interventions in metabolic risk can be tailored by sex. The hypothesis is that men, even at the early stage of schizophrenia, already demonstrate higher cardiovascular risk factors, which persist into the chronic phase. By contrast, women might have a different profile, with greater antidepressant use but less severe adverse metabolic profiles. Understanding these differences is essential for developing integrated, gender-sensitive intervention strategies to improve long-term outcomes for patients with schizophrenia [2, 1].

Methods

Study Design

This prospective cohort study was conducted at Aalborg University Hospital, Region North, Denmark, and was designed as a dual-part investigation. In the first part, we carried out a comprehensive clinical evaluation of somatic and psychiatric variables at baseline using rigorous, standardized protocols. This included detailed assessments of demographic information (e.g., age, gender, illness duration, and diagnosis subtype), somatic measures (such as body mass index, blood pressure, and fasting lipid profiles), and psychometric evaluations (using the Positive and Negative Syndrome Scale [PANSS], Clinical Global Impression [CGI] scale, and Global Assessment of Functioning [GAF]). In the second part, the study incorporates a longitudinal follow-up aimed at monitoring cardiovascular outcomes over time. Patients will be re-evaluated at regular intervals—approximately every three years—to capture any incident cardiovascular events, progression in metabolic abnormalities, and all-cause mortality. This follow-up will utilize both direct clinical re-assessments and registry data, thereby ensuring a comprehensive understanding of the long-term interplay between psychiatric status and cardiovascular health. The current paper focuses on the baseline data while outlining the planned follow-up strategy, which is integral for determining the prognostic value of early cardiometabolic risk factors and for informing potential gender-sensitive intervention strategies.

Study Population

Participants were recruited from both inpatient and outpatient psychiatric services between 2016 and 2018.

The inclusion criteria were:
- A confirmed ICD-10 diagnosis of schizophrenia (F20.x) or schizoaffective disorder (F25.x),
- Age 18 years or older,
- Residency within Region North, and
- Ability to provide informed consent.

Exclusion criteria were:
- Pregnancy or breastfeeding,
- Severe cognitive impairment preventing reliable participation,
- Acute psychotic decompensation that precluded safe assessment and
- Legal constraints such as involuntary detention that would limit research participation.

Illness duration was determined by reviewing the patients' medical records. Participants were classified into two subgroups: an early-stage group, defined as patients diagnosed within the past 2 years (n = 70), and a chronic group, defined as those with a diagnosis of 10 or more years (n = 165). A gap of 2–10 years was intentionally omitted to achieve clear differentiation between new-onset and long-standing cases.

Data Collection

Data were collected by trained clinical staff using a standardized protocol. The assessments included the following:

Demographic and Clinical Data

Demographic variables such as age, sex, and residential information were obtained through patient interviews and record review. Diagnosis subtypes were recorded as follows: paranoid schizophrenia (F20.0), unspecified schizophrenia (F20.9), other schizophrenia (F20.x), and schizoaffective disorder (F25.x). Illness duration was calculated from the date of first diagnosis to the date of baseline assessment.

Somatic Measurements

Anthropometric data, including height and weight, were measured to calculate BMI (kg/m^2). Blood pressure was measured using an automated sphygmomanometer after a minimum of five minutes' rest in a seated position. Systolic and diastolic blood pressures were recorded in mmHg. Fasting blood samples were collected to analyze lipid profiles (total cholesterol, LDL, HDL, and triglycerides), Hemoglobin A1c (HbA1c), and estimated glomerular filtration rate (eGFR). These assays were performed in the hospital's clinical laboratory according to standard protocols.

Comorbid Conditions and Medication Use

Comorbid somatic conditions (hypertension, diabetes, coronary artery disease, heart failure, hypercholesterolemia, and COPD) were identified from both patient interviews and electronic medical records. Medication use was recorded in detail. Antipsychotics were categorized as first-generation or second-generation. Second-generation antipsychotics were further stratified into low, moderate, and high cardiometabolic risk categories based on current literature [4] . Antidepressant use was documented, including specific classes such as SSRIs, SNRIs, tricyclic antidepressants, and monoamine oxidase inhibitors. In addition, data on other medications such as beta blockers, ACE inhibitors/ARBs, calcium channel blockers, and diuretics were collected.

Psychiatric Symptom Assessments

The Positive and Negative Syndrome Scale (PANSS) was administered to evaluate psychotic symptoms, including positive, negative, and general psychopathology subscales [15] . The Clinical Global Impression (CGI) scale provided an overall measure of illness severity, and the Global Assessment of Functioning (GAF) scale was used to assess both symptom severity and functional status. These scales were administered by clinicians experienced in standardized psychiatric assessment.

Statistical Analysis

Continuous variables are reported as means ± SD or medians with interquartile ranges (IQR), as appropriate. Group comparisons utilized Student's t-tests for normally distributed variables and

Mann–Whitney U-tests for non-parametric data. Categorical variables were analyzed using chi-square or Fisher's exact tests. A p-value < 0.05 was considered statistically significant. The analysis was conducted separately for the overall cohort, the early-stage subgroup (<2 years), and the chronic subgroup (≥10 years). Additionally, psychometric scales (PANSS, CGI, GAF) were compared between men and women across the entire cohort.

Results

A total of 235 patients were included in the analysis. The cohort was divided into 103 women and 132 men. For further stratification, 70 patients were classified as early-stage (diagnosed <2 years) and 165 as chronic (diagnosed ≥10 years).

Table 1. Overall Baseline Characteristics (N = 235)

Variable	Women (n = 103)	Men (n = 132)	p-value
Age (years) median [IQR]	45 [24.5, 55.5]	42 [31, 51]	0.4602
Diagnosis Subtype*	Paranoid (F20.0): 71 (71.0%) Unspec (F20.9): 6 (6.0%) Other (F20.x): 20 (20.0%) Schizoaffective (F25.x): 3 (3.0%) Missing: 3	Paranoid (F20.0): 84 (64.6%) Unspec (F20.9): 11 (8.5%) Other (F20.x): 27 (20.8%) Schizoaffective (F25.x): 8 (6.2%) Missing: 2	0.5730
Illness Duration (years) median [IQR]	16.7 [1.7, 24.4]	14.7 [1.9, 23.4]	0.9701
Antipsychotic Use (%)	90.3	92.4	0.7295
First-Generation AP (%)	14.6	12.9	0.8557
Second-Generation AP:			
Low Risk (%)	38.8	42.4	0.6733
Moderate Risk (%)	38.8	28.8	0.1380
High Risk (%)	31.1	37.9	0.3426
Antidepressant Use (%)	42.7	27.3	0.0193
SSRIs (%)	31.1	18.2	0.0318
SNRIs (%)	14.6	10.6	0.4745
Smoking Status (%):	Never: 26.4% Active: 44.0% Former: 29.7% Missing: 12%	Never: 26.4% Active: 52.9% Former: 20.7% Missing: 11%	0.2774
BMI (kg/m²) median [IQR]	29.2 [24.8, 33.6]	27.9 [24.6, 32.2]	0.1786
Overweight (%)	70.9	57.8	0.0761
Metabolic Syndrome (%)	55.3	63.1	0.3411

Systolic BP (mmHg) median [IQR]	119.5 [112.2, 129.8]	131 [123, 139]	<0.0001
Diastolic BP (mmHg) median [IQR]	81 [74.2, 87.8]	84 [77, 91]	0.0023
Heart Rate (bpm) median [IQR]	76 [67, 84]	76.5 [64.2, 85.8]	0.7317
Heart Failure (%)	0.0	1.5	0.5899
Coronary Artery Disease (%)	1.0	1.5	0.9990
Hypertension (%)	3.9	4.5	0.9990
Total Cholesterol (mmol/L) median [IQR]	4.4 [3.8, 5.2]	4.8 [4.2, 5.6]	0.0021
LDL Cholesterol (mmol/L) median [IQR]	2.3 [1.8, 2.7]	2.6 [2.0, 3.2]	0.0012
HDL Cholesterol (mmol/L) median [IQR]	1.3 [1.1, 1.6]	1.1 [0.9, 1.3]	<0.0001
Triglycerides (mmol/L) median [IQR]	1.5 [1.0, 2.2]	2.0 [1.1, 3.2]	0.0033
Hemoglobin A1c (mmol/L) median [IQR]	35 [32.0, 37.8]	34 [32, 37]	0.6373
Estimated GFR (mL/min/1.73 m²) median [IQR]	101.5 [91.9, 115.3]	104.9 [91.6, 112.4]	0.9042

Table 1 Description:
Table 1 summarizes the baseline demographic, clinical, and metabolic characteristics for the entire cohort of 235 patients diagnosed with schizophrenia or schizoaffective disorder, divided by sex (103 women and 132 men). Overall, several key findings emerge:

Age and Illness Duration:
The median age for women is 45 years (IQR: 24.5 to 55.5), whereas for men it is 42 years (IQR: 31 to 51). Despite a slight numerical difference, this difference is not statistically significant ($p = 0.4602$), suggesting that the overall age distribution is comparable between genders. Similarly, the median illness duration—16.7 years for women compared to 14.7 years for men—shows no significant difference ($p = 0.9701$). These findings indicate that any subsequent differences in metabolic or cardiovascular risk factors are unlikely to be explained by age or length of illness alone.

Diagnosis Subtypes:
The diagnosis subtypes were categorized into paranoid schizophrenia (F20.0), unspecified schizophrenia (F20.9), other schizophrenia (F20.x), and schizoaffective disorder (F25.x). In both men and women, paranoid schizophrenia is the most common subtype (71.0% in women and 64.6% in men). The distribution of subtypes does not differ significantly between women and men ($p = 0.5730$), indicating that the underlying psychiatric diagnoses are similar across gender groups.

This uniformity supports that observed metabolic differences are not attributable to diagnostic heterogeneity [12].

Antipsychotic Medication Use:
Overall, antipsychotic use is high, with 90.3% of women and 92.4% of men receiving treatment ($p = 0.7295$). Within antipsychotic categories, the proportions for first-generation agents are similar (14.6% in women versus 12.9% in men; $p = 0.8557$). For second-generation antipsychotics, while the use of agents with low cardiometabolic risk is comparable (38.8% vs. 42.4%, $p = 0.6733$), there is a non-significant trend towards a higher proportion of men being treated with agents classified as having moderate or high cardiometabolic risk (moderate risk: 38.8% in women vs. 28.8% in men, $p = 0.1380$; high risk: 31.1% vs. 37.9%, $p = 0.3426$). These data suggest that overall antipsychotic treatment patterns do not differ drastically between genders, though the trends may be clinically relevant when considering long-term metabolic impact [4].

Antidepressant Use:
One of the most notable findings in Table 1 is the significantly higher rate of antidepressant use among women (42.7%) compared to men (27.3%; $p = 0.0193$). This difference is further reflected in the use of selective serotonin reuptake inhibitors (SSRIs), with 31.1% of women receiving SSRIs versus 18.2% of men ($p = 0.0318$). The use of serotonin-norepinephrine reuptake inhibitors (SNRIs) is similar between groups ($p = 0.4745$). These findings may indicate that women are either more likely to experience comorbid depressive symptoms or that clinicians are more inclined to treat depressive symptoms in women.

Smoking Status:
Smoking status is similar between genders, with approximately 26.4% of each group identified as never smokers. Active smoking is reported in 44.0% of women and 52.9% of men, while former smoking is 29.7% in women and 20.7% in men; however, these differences are not statistically significant ($p = 0.2774$). This similarity suggests that lifestyle factors related to smoking may not account for the observed gender differences in cardiovascular risk factors.

Body Mass Index (BMI) and Overweight Prevalence:
The median BMI is 29.2 kg/m^2 in women and 27.9 kg/m^2 in men ($p = 0.1786$). Although a higher percentage of women (70.9%) are classified as overweight compared to men (57.8%), this difference approaches but does not reach statistical significance ($p = 0.0761$). These data indicate that although BMI values are numerically higher in women, this factor alone does not explain the metabolic differences observed between genders.

Blood Pressure:
Blood pressure differences are among the most striking findings. Women have a median systolic blood pressure of 119.5 mmHg, while men have a median of 131 mmHg; this difference is highly statistically significant ($p < 0.0001$). Diastolic blood pressure is also higher in men (84 mmHg) compared to women (81 mmHg, $p = 0.0023$). Elevated blood pressure is a critical risk factor for CVD, and these findings are consistent with the literature indicating that men are predisposed to higher blood pressure [10].

Lipid Profile:
Lipid parameters further differentiate the groups. Women have lower total cholesterol (median 4.4 mmol/L) compared to men (4.8 mmol/L, p = 0.0021). LDL cholesterol is also significantly lower in women (median 2.3 mmol/L) than in men (2.6 mmol/L, p = 0.0012). Importantly, HDL cholesterol is significantly higher in women (median 1.3 mmol/L) than in men (1.1 mmol/L, p < 0.0001). Additionally, triglyceride levels are lower in women (median 1.5 mmol/L) compared to men (median 2.0 mmol/L, p = 0.0033). These lipid profile differences are crucial because higher total cholesterol, higher LDL, and higher triglycerides, combined with lower HDL, are well-established risk factors for cardiovascular disease [14].

Glycemic Control and Renal Function:
There are no significant gender differences in hemoglobin A1c (median 35 mmol/L in women vs. 34 mmol/L in men, p = 0.6373) or estimated glomerular filtration rate (eGFR; p = 0.9042), suggesting that glycemic control and renal function are relatively similar between women and men in this cohort.

Summary:
In summary, Table 1 illustrates that while the overall demographic characteristics (age, illness duration, BMI, smoking status) and psychiatric diagnostic profiles are comparable between genders, significant differences exist in terms of cardiometabolic risk factors. Men show a notably worse cardiovascular risk profile, with higher blood pressure and a less favorable lipid profile, which could predispose them to increased CVD risk over time. Conversely, women are more likely to receive antidepressants, particularly SSRIs, indicating potential differences in comorbid psychiatric symptoms. These baseline differences provide critical insights into the need for gender-specific screening and early intervention strategies in patients with schizophrenia [1, 2].

Table 2. Baseline Characteristics for Early-Stage Schizophrenia (<2 Years, n = 70)

Variable	Women (n = 32)	Men (n = 38)	p-value
Age (years) median [IQR]	21.5 [20.0, 23.2]	26.5 [22.0, 29.0]	<0.0001
Illness Duration (years) median [IQR]	0.9 [0.4, 1.5]	1.1 [0.8, 1.5]	0.0818
Antipsychotic Use (%)	78.1	97.4	0.0320
Systolic BP (mmHg) median [IQR]	113 [106.8, 118.5]	130 [120, 137]	<0.0001
Diastolic BP (mmHg) median [IQR]	75.5 [70.2, 81.8]	78 [74.8, 89.0]	0.0426
HDL Cholesterol (mmol/L) median [IQR]	1.2 [1.1, 1.3]	1.0 [0.9, 1.1]	0.0295
Triglycerides (mmol/L) median [IQR]	1.6 [1.0, 2.0]	2.4 [1.3, 3.0]	0.0430

Table 2 Description:
Table 2 focuses on 70 patients with early-stage schizophrenia (diagnosed <2 years), comprising 32 women and 38 men. The analysis reveals a statistically significant age difference: women have a median age of 21.5 years while men have a median age of 26.5 years ($p < 0.0001$), suggesting that men are generally diagnosed at a slightly later age in this subgroup. Illness duration does not differ significantly between genders, ensuring comparability regarding time since diagnosis. Notably, antipsychotic use is significantly higher in men (97.4%) than in women (78.1%, $p = 0.0320$), which may predispose men to early metabolic disturbances. In addition, men display significantly elevated systolic blood pressure (median 130 mmHg versus 113 mmHg in women, $p < 0.0001$) and a less favorable lipid profile, evidenced by lower HDL levels (median 1.0 mmol/L vs. 1.2 mmol/L, $p = 0.0295$) and higher triglyceride levels (median 2.4 mmol/L vs. 1.6 mmol/L, $p = 0.0430$). These findings indicate that even early in the disease course, men exhibit a more adverse cardiovascular risk profile, underscoring the need for prompt, gender-specific screening and intervention strategies.

Table 3. Baseline Characteristics for Chronic Schizophrenia (≥10 Years, n = 165)

Variable	Women (n = 71)	Men (n = 94)	p-value
Age (years) median [IQR]	53 [44.5, 60.0]	48 [40.0, 53.8]	0.0032
Illness Duration (years) median [IQR]	20.9 [15.9, 26.4]	19.4 [14.2, 26.5]	0.4986
Antipsychotic Use (%)	95.8	90.4	0.3138
Systolic BP (mmHg) median [IQR]	122 [116.8, 133.2]	132.5 [125.2, 141.0]	0.0010
Diastolic BP (mmHg) median [IQR]	83 [77.8, 89.0]	86.5 [80.0, 92.0]	0.0155
Total Cholesterol (mmol/L) median [IQR]	4.4 [4.0, 5.1]	4.8 [4.4, 5.6]	0.0090
LDL Cholesterol (mmol/L) median [IQR]	2.3 [1.8, 2.7]	2.5 [2.1, 3.3]	0.0011
HDL Cholesterol (mmol/L) median [IQR]	1.5 [1.1, 1.8]	1.1 [0.9, 1.4]	<0.0001
Triglycerides (mmol/L) median [IQR]	1.4 [0.9, 2.2]	1.9 [1.1, 3.2]	0.0255
Antidepressant Use (%)	49.3	31.9	0.0356

Table 3 Description:
Table 3 presents baseline characteristics for 165 patients with chronic schizophrenia (diagnosis ≥10 years), including 71 women and 94 men. Although women in this group are significantly older than men (median 53 vs. 48 years; $p = 0.0032$), men consistently exhibit higher cardiovascular risk.

Specifically, men have significantly elevated systolic blood pressure (median 132.5 mmHg vs. 122 mmHg; p = 0.0010) and diastolic blood pressure (median 86.5 mmHg vs. 83 mmHg; p = 0.0155). These blood pressure differences suggest a persistent risk for cardiovascular morbidity in men despite shorter time since diagnosis.

The lipid profile further differentiates by sex. Men demonstrate higher total cholesterol (median 4.8 mmol/L vs. 4.4 mmol/L; p = 0.0090) and LDL cholesterol (median 2.5 mmol/L vs. 2.3 mmol/L; p = 0.0011) along with significantly lower HDL cholesterol (median 1.1 mmol/L vs. 1.5 mmol/L; p < 0.0001) and higher triglycerides (median 1.9 mmol/L vs. 1.4 mmol/L; p = 0.0255). These findings indicate a more atherogenic lipid profile in men, contributing to their increased cardiovascular risk (Pletcher et al., 2004).

Additionally, antidepressant use is significantly higher among women (49.3% vs. 31.9%, p = 0.0356), suggesting differences in comorbid mood symptom management. In summary, despite similar time since diagnosis, chronic-phase men exhibit a distinctly adverse cardiovascular risk profile compared with women, emphasizing the need for gender-specific screening and intervention strategies.

Table 4. Psychometric Scales for All Participants (N = 235)

Variable	Women (n = 103)	Men (n = 132)	p-value
PANSS Total (mean ± SD)	62.1 ± 17.5	62.0 ± 18.9	0.9961
PANSS Positive (mean ± SD)	15.9 ± 5.6	15.7 ± 6.4	0.8554
PANSS Negative (mean ± SD)	15.4 ± 6.5	16.4 ± 6.8	0.2869
PANSS General (mean ± SD)	30.8 ± 8.7	30.3 ± 8.7	0.7083
CGI (mean ± SD)	3.6 ± 0.9	3.7 ± 1.2	0.6019
GAF Symptom (mean ± SD)	43.2 ± 11.0	43.4 ± 10.9	0.8833
GAF Function (mean ± SD)	48.0 ± 10.0	46.4 ± 9.9	0.2458

Table 4 Description:
Table 4 presents psychometric data for the entire cohort (n = 235), comparing women and men using PANSS subscales, CGI, and GAF scores. Overall, there are no statistically significant differences between genders in the severity of psychotic symptoms or global functioning. Specifically, the PANSS total and subscale scores (positive, negative, and general) are nearly identical between women and men (p-values ranging from 0.7083 to 0.9961), and both CGI and GAF scores are also comparable (p > 0.2458). These results indicate that the overall psychiatric symptom burden is equivalent across genders. Consequently, the marked cardiovascular disparities observed in our study appear to be independent of psychosis severity, underscoring that the increased cardiovascular risk in men is likely driven by other factors, such as differential medication exposure and lifestyle behaviors, rather than differences in psychiatric symptomatology. This finding aligns with previous research [1,12] and emphasizes the importance of addressing cardiovascular risk separately from psychiatric symptom management in schizophrenia.

Discussion

Our study provides a comprehensive evaluation of cardiovascular risk factors and psychiatric symptom severity in a cohort of 235 patients with schizophrenia or schizoaffective disorder, stratified by both sex and time since diagnosis. The results reveal that, despite a similar overall psychiatric burden between men and women—as evidenced by equivalent scores on the PANSS, CGI, and GAF scales—there exist marked differences in somatic risk factors that may help explain the well-documented excess cardiovascular morbidity and mortality in this population [1, 2].

In our overall sample (Table 1), the median systolic and diastolic blood pressures were significantly higher in men compared with women. Specifically, men exhibited a median systolic blood pressure of 131 mmHg compared with 119.5 mmHg in women, and a median diastolic pressure of 84 mmHg versus 81 mmHg in women. These findings align with earlier epidemiological data in the general population showing that men are predisposed to higher blood pressures [10, 14]. Additionally, the lipid profile of men was notably less favorable: men had significantly higher total cholesterol and LDL cholesterol, as well as higher triglyceride levels, while HDL cholesterol was significantly lower than in women. This combination of dyslipidemia is a well-known predictor of atherosclerotic cardiovascular disease [14] and underscores the potential contribution of adverse lipid metabolism to the elevated cardiovascular risk observed in men with schizophrenia.

When we examined the early-stage subgroup (diagnosis <2 years, Table 2), the gender differences were particularly pronounced. Men in this subgroup not only were significantly older at evaluation (median 26.5 years vs. 21.5 years in women, $p < 0.0001$) but also had a near-universal rate of antipsychotic use (97.4% vs. 78.1%, $p = 0.0320$). This early high exposure to antipsychotic medication, known to induce weight gain and metabolic disturbances [4], may contribute to the higher blood pressure and less favorable lipid profiles seen in men even at the initial stages of the disorder. The early appearance of these cardiovascular risk factors in men suggests that metabolic dysregulation may be an inherent part of the disease process or a result of early treatment effects, as supported by previous studies [6, 8]. Conversely, the early-stage data also reveal that women, while being younger and less frequently treated with antipsychotics, maintain a more favorable cardiovascular profile. These observations reinforce the concept that gender-specific differences in cardiovascular risk factors are apparent from the early phases of schizophrenia, highlighting an important window for early intervention.

In the chronic subgroup (diagnosis ≥10 years, Table 3), the differences between genders continue to persist. Although women in this group are significantly older (median 53 years) compared with men (median 48 years, $p = 0.0032$), men still exhibit significantly higher systolic and diastolic blood pressures (median 132.5 mmHg vs. 122 mmHg, $p = 0.0010$; 86.5 mmHg vs. 83 mmHg, $p = 0.0155$, respectively). In addition, the lipid profiles remain significantly different, with men having higher total and LDL cholesterol and lower HDL levels, as well as higher triglycerides. These chronic-phase findings are consistent with research in both the general population and in schizophrenia samples, suggesting that the adverse cardiovascular risk in men is not only an early phenomenon but also persists over time [10, 7]. Notably, women in the chronic group were more likely to be prescribed antidepressants (49.3% vs. 31.9%, $p = 0.0356$), which may indicate a differential pattern of comorbidity, with a potentially greater prevalence or recognition of depressive symptoms among women [8].

Our psychometric data (Table 4) further highlight that, despite these significant somatic differences, the severity of psychotic symptoms remains essentially equivalent between genders. The PANSS total score, as well as its positive, negative, and general subscales, showed no significant differences between women and men. Similarly, CGI and GAF scores were comparable across gender groups. This dissociation between the somatic and psychiatric domains suggests that while the overall burden of psychotic symptoms may be similar, the physical health risks associated with schizophrenia—especially the heightened cardiovascular risk in men—are driven by factors that are independent of psychosis severity. These results support previous findings indicating that metabolic and cardiovascular risk factors in schizophrenia are not directly correlated with the severity of psychotic symptoms [1, 12].

Our study contributes to the growing body of literature by providing detailed, stratified data on cardiovascular risk factors in schizophrenia. The robust differences in blood pressure and lipid profiles between men and women, present from the early stages of illness and persisting in chronic disease, underscore the importance of early and continuous cardiovascular monitoring in patients with schizophrenia. Moreover, the high prevalence of antipsychotic use and the significant differences in antidepressant prescriptions raise important questions about the role of psychotropic medications in modulating cardiovascular risk. These findings resonate with earlier studies that have demonstrated the metabolic side effects of antipsychotic medications and their contribution to increased cardiovascular morbidity in schizophrenia [4, 5].

There are some limitations to our study. First, although our sample size allowed for meaningful stratification by gender and illness duration, the study was conducted at a single center, which may limit the generalizability of our findings. Second, while our comprehensive baseline assessments included a broad range of metabolic and psychiatric parameters, there remains the potential for unmeasured confounding factors such as physical activity levels and dietary habits that were not systematically captured. Finally, our cross-sectional baseline data cannot establish causality, although the planned longitudinal follow-up will enable us to track changes in cardiovascular risk factors and their relationship with clinical outcomes over time.

Conclusion

In summary, our prospective study of 235 patients with schizophrenia demonstrates that men exhibit a significantly higher cardiometabolic risk compared with women, as evidenced by higher blood pressure, more adverse lipid profiles, and elevated triglyceride levels. These differences are apparent both in early-stage and chronic schizophrenia, indicating that men's heightened cardiovascular risk develops early and persists over time. In contrast, the severity of psychotic symptoms, as measured by PANSS, CGI, and GAF, does not differ by gender, suggesting that the metabolic risks are independent of the clinical severity of psychosis.
These findings highlight the critical need for integrated, gender-sensitive screening and intervention strategies that address both psychiatric and cardiovascular health from the earliest stages of schizophrenia. By targeting metabolic risk factors early—particularly in men—clinicians may reduce the excessive cardiovascular morbidity and mortality associated with this disorder. Future research should focus on longitudinal assessments and the implementation of targeted

interventions that combine lifestyle modifications, medication adjustments, and close monitoring of cardiovascular risk in schizophrenia patients.

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